Prescribing for children

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10.12968/npre.2018.16.7.341

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Abstract

In this article in the series of ‘bite sized’ pharmacology, we will look at the pharmacological considerations when prescribing for children. This article will illustrate the common issues to consider when prescribing for the under 18 (or more often than not the under 12) population. The primary focus will be on pharmacokinetics and the four processes that occur after oral drug administration, with specific details on the factors that affect these processes in this patient group. There will also be some consideration of legal aspects and consent to treatment including concordance and a brief area on licensing. Exercises provided will help you apply this knowledge to your prescribing practice.

We must remember as prescribers that a drug has to be:

- Available in a suitable form
- Administered by an appropriate route
- Absorbed into the body fluids and tissues
- Distributed to its active site
- Metabolised, primarily by the liver
- Excreted, primarily by the kidneys

These actions that occur after administration are pharmacokinetics and we shall begin by exploring the differences in this population of patient as this is an area of significant consideration for the prescriber.

Pharmacokinetics is the action of the body on the drugs that we take. It can be broken down into four processes as can be seen from table 1. (More detail on each of these processes is found in the article on pharmacokinetics in Volume 15, issue3).

Table 1- The four pharmacokinetic processes that occur after oral drug administration

A- Absorption of the drug
D- Distribution of the drug molecules
M- Metabolism of the parent drug
E- Excretion of the drug and its metabolites

As we have done in a previous article in this series (Robertson, D. 2018), we will consider the seven principles of good prescribing practice when dealing with children.

Prescribing Pyramid (NPC 1999)

When considering prescribing for children, it is important to remember that dependent on the age and understanding of the child, information may need to be gathered in a different way, from someone other than the child themselves, and how you interpret and use this information may be different. We will go on to explore the relevant areas of this framework.

Exercise

Using the BNF, look up the section on prescribing in children. Review all the areas it discusses and reflect on how these may correlate with your area of prescribing.

Consider the Patient

Consideration of the patient should be modified to reflect the additional considerations required in the child. The age of the child and their stage of development both emotionally, physically and cognitively need to be factored in.

The main factors to consider in addition to normal consultation and examination are;

- Development of the normal pharmacokinetic processes
- Small size and weight
- Formulation of medication
- Ability of child to take medication
- Compliance considerations- child and responsible adult
- School and medicine administration issues

Pharmacokinetics Considerations

Absorption

Absorption of drugs from all administration routes except intravenous is required to get the drug from the site of administration to the blood stream. There are some specific considerations when prescribing in children.

There can be some issues in using the oral route of administration

- In young infants, gastric emptying time is often prolonged and only approaches adult values at around 6 months of age.
- Increased gastric pH: gastric acid output does not reach adult values until the second year of life so the gastric fluid environment is not as acidic.
- Other factors: gastrointestinal contents (related to feeding; especially if ‘demand’ feeding, and stage of weaning), posture (position of child and head stability related to age and

development), disease states (for example pyloric stenosis or infant reflux) and therapeutic interventions, such as drug therapy or feeding tubes, can also affect the absorption process.

- Some children, of many ages have problems swallowing tablets and this may mean that either liquid preparations should be considered or if severe problems encountered, then another route of administration may be required.

Distribution

Distribution of drugs from the plasma to cell and tissues can be compromised due to any or a combination of the following factors

- Increased total body water: as a percentage of total body weight, the total body water and extracellular fluid volume of the child decreases with increasing age. Neonates require higher doses of water-soluble drugs, on an mg/kg basis, than adults.

- Decreased plasma protein binding: plasma protein binding in neonates is reduced as a result of low levels of albumin and globulins and an altered binding capacity meaning that there is more ‘free drug’ available and dosing should be considered to allow for this to avoid toxicity.

- The presence of high levels of bilirubin in the circulation of the neonate can affect binding to plasma proteins, this is usually only a problem in the first few days of life as the liver function increases and adapts, even in the child not needing phototherapy for high bilirubin levels but with a degree of jaundice present.

- Neonates have less efficient skin barrier meaning topical preparations are more readily absorbed and they have a more permeable blood-brain barrier allowing easy passage of drugs into the central nervous system

Metabolism

Drug metabolism primarily occurs in the liver

- Enzyme systems mature at different times and may be absent at the time of birth, or present in considerably reduced amounts, especially in pre-term infants. This can be compounded if there a high levels of circulating bilirubin as the liver adapts to its role in the independent baby as oppose to the dependent foetus.
- Cytochrome P450 metabolic enzyme expression is lower in neonates and increases with age and development. Adult values can be reached by an average of 2 years of age. Some drug metabolising enzymes for certain drugs, such as the phenobarbital, take longer to mature and prescribing for these drugs should be done with caution (Ku & Smith 2015)

Excretion

- Glomerular filtration, active tubular secretion and tubular reabsorption reduced at birth but clearance increases with age to near adult values by 6-12 months in the term infant.
- Lower values are seen in pre term infants and maturation occurs later

(Ku & Smith 2015)

Pharmacological considerations may influence the 'Choice of Product' area of the framework and impact on the 'Strategy' and 'Negotiate a Contract' aspects also.

Exercise

Using the BNF, or other drug resource, look up a drug you are likely to prescribe in practice. Identify if there are any restrictions on prescribing in children, infants or neonates. Reflect on any changes you would need to make to dose or prescribing regimes in light of this.

Other Areas to be Aware of

Dosages and Dosing Regimens

- Paediatric doses should be obtained from a paediatric dosage reference text, such as the BNFC or local paediatric formularies and not extrapolated from the adult dose.
- Unless the age is specified, the term 'child' in the BNFC includes persons aged 12 years and younger. This can be broken down into prescribing age ranges as follows;
    - neonate (birth to 1 month)
    - infant (1 month to 2 years)
    - child (2 to 12 years)

Compliance and Concordance

Compliance with the prescribed medication in children can be influenced by many factors, which often differ from factors that affect adult compliance with medication. Children may not be able themselves to consent to medication taking and often the parent or guardian is approached for consent. In an older child it may be appropriate to check capacity to consent using Fraser Guidelines to see if the child is Gillick competent in their acceptance or refusal of treatment (Gillick 1984).

We should still always try to reach a concordant agreement and this falls under the 'Negotiate a Contract' section of the prescribing pyramid. It should also be considered at the 'Review' stage.

- Compliance in children can be influenced by the formulation, taste, appearance and ease of administration of a preparation.

- Prescribed regimens should, where possible be tailored to the child's daily routine accounting for age appropriate factors such as school or nursery and feeding regimes.
- Treatment goals should be set in collaboration with the child where it is feasible to do so, or with the parent or guardian where this is more appropriate.
- Whenever possible, the use of products which avoid the need for administration during school hours should be considered (e.g. modified-release preparations or drugs with long half-lives). When administration at school is unavoidable, consideration should be given to the information and supply to conform to school regulations.
- Children with ongoing need for medication due to long term conditions should have a health care plan for school.
- Avoid painful intramuscular injections where possible

Exercise

Can you identify factors for the children in your area of practice that might affect their ability to comply with or adhere to the medication regimes? Reflect on how you could manage these from a pharmacological and prescribing perspective.

Product Licensing

The BNF states that wherever possible, medicines for children should be prescribed within the terms of the marketing authorisation, also known as the product license. It is however widely acknowledged that many medications are not specifically licensed for paediatric use and this has to be taken into account by the prescriber when prescribing medications that are needed but have no specific paediatric license. It is recognised and accepted that the informed use of licenced medicines out with the terms of their product licence (off-license or off-label use) is often necessary in paediatric practice.

Prescription Writing

There are specifics with regards to prescription writing requirements in primary care for the child under 12. This comes under the ‘Record Keeping’ area of the pyramid.

- Inclusion of age on the prescription FP-10 is a legal requirement in the case of prescription-only medicines for children under 12 years of age. It is good practice to state the age for all prescriptions for children. If the child is under 5 years old, then the age must be stated in years and months.
- Wherever appropriate the prescriber should state the current weight of the child to enable the dose prescribed to be checked.
- It is important to state the strengths of capsules or tablets or liquid medication and prescribe the dose to be given e.g. in mg rather than the amount in ml
- Liquid preparations may contain sugar which encourages dental decay. Sugar-free medicines are preferred for long-term treatment.

Adverse Drug Reactions & Reporting In Children

As with other patients the reporting of suspected adverse drug reactions should be done via the Yellow Card Scheme. The identification of adverse effects in children is particularly important as the effects pharmacologically in children may differ from those in adults. We have less knowledge around a child’s response to medications as many drugs have not been tested in children. The effects of a drug on a child’s growth and development can be seen as delayed adverse reactions and may be reported after the fact.

Exercise

Using a BNF or other resource identify any specific prescription writing requirements for a drug from your area of practice in a child or neonate. Then go on to identify if possible any special licensing information for paediatric use.

Suggested and Further Reading

Barber and Robertson (2015) *Essentials of Pharmacology for Nurses* 3rd Edition McGraw Hill London

BNF Online https://www.bnf.org/products/bnf-online/

Electronic Medicines Compendium https://www.medicines.org.uk/emc/

Gillick v West Norfolk and Wisbech Area Health Authority and Department of Health and Social Security [1984] Q.B. 581.

Ku, L.C. & Smith, P.B. (2015) Dosing in neonates: *Special considerations in physiology and trial design* Pediatr Res 77(0):2-9

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